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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/541,277	06/08/2006	Friedhelm Brassel	13455/1	6606

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EXAMINER	
ARNOLD, ERNST V	
ART UNIT	PAPER NUMBER
1616	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/541,277	BRASSEL, FRIEDHELM	
	Examiner	Art Unit	
	ERNST V. ARNOLD	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/17/09 has been entered.

Claims 17-29 are pending and under examination.

Withdrawn rejections:

Applicant's amendments and arguments filed 4/17/09 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed below is herein withdrawn. Claims 17-29 were rejected under 35 U.S.C. 103(a) as being unpatentable over Doerfler et al. (Neuroradiology 2001, 43, 1112-1117) in view of Mottu et al. (Biomaterials, 2000, 21, 803-811). This rejection is withdrawn in favor of the following rejection with the newly found art of Rump et al. (Eur J Clin Pharmacol 2002, 58, 459-465).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 17-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 17 and 22 introduce new matter as the claims recite the limitation: "comprising" There is no support in the specification for this limitation. The limitation of: "comprising" was not described in the specification as filed, and person skilled in the art would not recognize in the applicant's disclosure a description of the invention as presently claimed. The specification only mentions the term 'comprising' on page 5, lines 11-12, in reference to the three component embolizate and not a medical kit, and again on page 3, lines 16-17, with respect to: "Ethibloc® comprises a primary contrast medium". Original claim 15 filed on 06/30/05 is drawn to a medical kit contains components (a), (b), and (c) according to any one of claims 1 to 5. Claim 1 recites "consisting of" and claims 3 and 5 recite "consists of". As filed, the medical kit is limited to a liquid embolizate that consists of certain elements. Therefore, expanding the scope of the medical kit to comprising language for the liquid embolizate represents a new concept not previously presented and is new matter.

There is no guidance in the specification to select "comprising" and from MPEP 2163.06: "Applicant should therefore specifically point out the support for any amendments made to the disclosure." Applicant has not directed the Examiner to the support in the specification for the amendments. Therefore, it is the Examiner's position that the disclosure does not reasonably convey that the inventor had possession of the subject matter of the amendment at the time of filing of the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 17-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rump et al. (Eur J Clin Pharmacol 2002, 58, 459-465) in view of Doerfler et al. (Neuroradiology 2001, 43, 1112-1117)

Applicant claims a medical kit for use in a method to produce a liquid embolizate ready for use in a method for treatment vascular malformations, said liquid embolizate comprising: (a) 20 to 80% v/v of an occlusion mixture containing a zein emulsion in aqueous ethanol, (b) 10 to 40% v/v of a radiopaque contrast medium in liquid form and (c) 10 to 40% v/v of ethanol, the percentages of components (a), (b) and (c) adding up to 100% of the liquid embolizate, components (a), (b) and (c) being separately packed and drawn-up into syringes, the kit further including at least one empty syringe for accommodation of the readily prepared liquid embolizate and a three-way cock..

Determination of the scope and content of the prior art

(MPEP 2141.01)

Rump et al. teach sealing the hepatic artery by injection of 0.2-0.5 ml Ethibloc emulsion consisting of (8 ml Ethibloc, 1.5 ml Lipiodol, and 1.5 ml ethanol) (Page 461, left column second paragraph). The total volume would be 8 + 1.5 + 1.5 = 11 ml. thus the v/v% would be about:

Ethibloc = 8/11 X 100% = 72.7%

Lipiodol = 1.5/11 X 100% = 13.6%

Ethanol = 1.5/11 X 100% = 13.6%

Thus, the art fairly teaches an occlusion mixture containing a zein emulsion (Ethibloc) in aqueous ethanol with a radiopaque contrast medium (Lipiodol) and further containing ethanol within the amounts instantly claimed. The volume ratio of lipiodol to ethanol is 1:1 which is between 1:2 and 2:1.

Doerfler et al. is relied upon for teaching Ethibloc (60% ethanolic zein) and Lipiodol compositions in ratios of E/L 1:1, 1:2 and 1:3) (Abstract and page 1113, table 1 and Ethibloc right column). Doerfler et al. teach injection through a microcatheter is not smooth because of Ethibloc's high viscosity and to decrease the viscosity by mixing with the oily contrast medium Lipiodol (page 1113, right column Ethibloc). From page 1113:

> Ethibloc (Ethicon, Norderstedt, Germany) is an ethanolic (60%) solution of 210 mg zein (corn protein)/ml ethanol, 162 mg sodium amidotrizoate/ml ethanol, 145 mg oleum papaveris/ml ethanol and 6 mg propyleneglycol/ml ethanol. As the alcohol dissolves in aqueous media, zein precipitates and forms a cast with a consistency resembling "chewing gum".
>
> Injection through a microcatheter is not smooth, because of Ethibloc's high viscosity. To decrease this high viscosity and to enhance visibility under fluoroscopy, Ethibloc can be mixed with the iodinated contrast agent Lipiodol in different solutions.

Oleum papaveris is another term for poppy seed oil. Amidotrizoate is a radiopaque agent. Methods of mixing Ethibloc in 3-way tap with Lipiodol with 1 cc syringes are taught (page 1113, study design). Doerfler et al. teach that the high viscosity of Ethibloc can become a problem with certain microcatheters which rupture while the embolic agent is injected (page 1115, lower right paragraph through page 1116). Doerfler et al. teach embolization of arteriovenous malformations (Introduction, page 1112) and cerebral malformations as well as capillary embolization of the kidneys (page 1113, left column).

Doerfler et al. establish two things: 1) Ethibloc is highly viscous and problematic for injection and 2) Lipiodol is a known contrast medium in liquid form.

Ascertainment of the difference between the prior art and the claims

(MPEP 2141.02)

1. The difference between the instant application and Rump et al. is that Rump et al. do not expressly teach a medical kit comprising components (a), (b), and (c) being separately packed and drawn up into syringes and at least one empty syringe for accommodation of the liquid embolizate and a 3-way cock. This deficiency in Rump et al. is cured by the teachings of Doerfler et al.

2. The difference between the instant application and Rump et al. is that Rump et al. do not expressly teach a liquid embolisate that consists of 30 to 70% v/v of component (a) and 15 to 35% v/v each of components (b) and (c).

3. The difference between the instant application and Rump et al. is that Rump et al. do not expressly teach a method of producing a liquid embolizate with 3 components comprising in the absence of air, component (a) is homogenized, component (b) admixed with component in (a) and component (c) is admixed to the mixture comprising components (a) and (b).

Finding of prima facie obviousness

Rational and Motivation (MPEP 2142-2143)

1. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to make a medical kit with components (a), (b), and (c) being separately packed and drawn up into syringes and at least one empty syringe for

accommodation of the liquid embolizate and a 3-way cock, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because each of the solutions have to be stored somewhere and Doerfler et al. teach methods of mixing Ethibloc in 3-way tap with Lipiodol using syringes (page 1113, study design) which provides an easy and convenient means to store the solutions, quickly mix the solutions for use, and use the empty syringe to hold the mixed solution just before injection. Therefore, in the absence of evidence to the contrary, storage of the components in 3 separate syringes and having a fourth syringe for injecting the mixed solution would be obvious to one of ordinary skill in the art.

2. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to make a kit out of the composition of Rump et al. with the liquid embolisate that consists of 30 to 70% v/v of component (a) and 15 to 35% v/v each of components (b) and (c) and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because of the following rationale. A range of from 15 to 35% represents a 2.3-fold increase from 15-35% and there is no demonstration in applicant's specification that the recited range provides unexpected results. Since the addition of the ethanol affects the viscosity and the dispense force needed in such a way to afford the composition to be readily injected, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to add an amount of alcohol to the composition necessary to lower the dispense force in order to allow the composition to be injected. One having

ordinary skill in the art would have been motivated to optimize the composition by using an amount of ethanol that is expected to lower the viscosity and that would provide a composition that is easily injected directly to the application site. In the absence of factual evidence, 15-35% v/v of components (b) and (c) is not inventive over the prior art that uses 13.6% v/v of components (b) and (c).

3. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to add more ethanol to make the composition of Rump et al. wherein (a) is homogenized; (b) is admixed with (a) and (c) is then admixed to (a) and (b), and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because the solution has to mixed in some manner and it is merely a matter of pre-mixing the Ethibloc solution and adding the other components to produce the product. With respect to the limitations of mixing under vacuum; eliminating air by centrifuging, having the components in separately packed form and intermixed with the help of a mixing system (3-way cock), present in drawn up syringes and selecting occlusions of vessels, vascular malformations, aneurysms or arteriovenous short circuits these are merely judicious selection of experimental design choices or applications by one of ordinary skill in the art, especially in view of the teachings of Doerfler et al., in the absence of evidence to the contrary. The cited art already teaches injection of the solutions with syringes as well as the use of 3 way cocks and it is merely a design choice to have all the solutions packed in syringes and use the 3 way cock in the absence of evidence to the contrary.

From recent case law: "the results of ordinary innovation are not the subject of exclusive rights under the patent laws." (KSR INTERNATIONAL CO. v. TELEFLEX INC. ET AL. 550 U. S. ____ (2007) page 24).

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976).

In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Response to arguments:

Applicant's arguments are moot in view of the new ground of rejection.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ernst V. Arnold whose telephone number is 571-272-8509. The examiner can normally be reached on M-F (7:15 am-4:45 pm).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Ernst V Arnold/
Examiner, Art Unit 1616